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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,994	05/08/2000	MASAKI YUI	KP-8753	9126

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EXAMINER
SCHNIZER, HOLLY G

ART UNIT	PAPER NUMBER
1653	12

DATE MAILED: 06/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/509,994	YUI ET AL.	
	Examiner	Art Unit	
	Holly Schnizer	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 May 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

Claims 1-21 are pending. Claims 20-21 are withdrawn from consideration as being drawn to a non-elected invention for the reasons provided in the previous Office Action (Paper No. 10) and below. Therefore, Claims 1-19 will be considered in this Office Action.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-19 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the International examiner did not find a lack of unity therefore a lack of unity should not be found in the national case and that the lack of unity does not comply with PCT Rules 13.1 and 13.2 because the "special technical feature" is art based and therefore the lack of unity would require citation of a reference. This is not found persuasive because as stated in the previous Office Action, the special technical feature of Group I is maintaining the quality of an aqueous injection solution of thrombomodulin during storage and transportation while the special technical feature of Group II is a method of treatment to maintain soluble thrombomodulin in the blood. Since the special technical feature of Group I is not present in the Group II invention being claimed and the special technical feature of the Group II invention is not present in the Group I invention being claimed, unity of invention is lacking. The instant application contains multiple processes (method of maintaining the storage of a thrombomodulin solution (clms 1-11) and method of treatment (clms 20-21) and a product. If multiple processes and products are claimed,

the first invention of the category (product, process, use or apparatus) first mentioned in the claims (in this case the method of maintaining the quality of a thrombomodulin solution) and the first recited invention of each of the other categories related thereto (the thrombomodulin solution used in the method of maintaining the quality of a thrombomodulin solution) will be considered as the main invention. The process of treatment of Group II is not considered related to Group I because it has a different special technical feature as explained above. In response to Applicant's argument that citation of a reference is required to make the lack of unity; such reference is not required as explained above. However, it is noted that the method of Group I is unpatentable over Kunihiro et al. (U.S. Patent No. 5,202,421, Apr. 1993) for the reasons described below and therefore the technical feature of Group I is not considered a "special technical feature" because it is not a contribution over the prior art.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Priority

The present Application is a 371 of PCT JP98/04609. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Abstract

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Objections

Claim 1 is objected to for the recitation "quality of aqueous injection preparation" in lines 1-2. The claim should be amended to "an aqueous injection preparation".

Claim 17 is objected to for the misspelling of "buffer" in line 3.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 are indefinite as to what is being claimed. Is it a method of maintaining the quality of a thrombomodulin solution or a method of preparing a thrombomodulin solution. The claims are drawn to "a method for maintaining the quality of an aqueous injection preparation of thrombomodulin" yet there is only one step involving preparation of an aqueous solution of thrombomodulin and there is no endpoint to determine whether the method has achieved its goal. What actual steps,

besides preparing the thrombomodulin solution, are necessary for maintaining the quality of the solution, and what measurable value indicates that the thrombomodulin solution has maintained its quality?

Claims 1-11 are indefinite as to the metes and bounds of when the methods have been practiced successfully (e.g. when the method "maintains the quality" of the thrombomodulin preparation). The quality of a product is a qualitative property and not quantitative. There is no definition in the specification or in the claims as to when a thrombomodulin preparation is considered to have "maintained quality". Does "maintaining the quality" mean maintaining a particular activity of the thrombomodulin and if so, what range of activity would a preparation that has "maintained quality" have?

Claims 1-19 are indefinite because Claims 1-4 and12-14 recite "effective amount of a soluble thrombomodulin" without providing what effect the thrombomodulin is intended to have so that one could determine when the amount is "effective". Thus, the metes and bounds of the claims are unclear. Claims 5-11 and 15-19 are also indefinite because they depend from these indefinite claims but do not correct the deficiency. Correction is required.

Claims 1-9, 11, and 13-17, and 19 are indefinite as to the metes and bounds of "substantial" gas space. The term "substantial" in claims 1, 3-4, 13-14, and 18 is a relative term which renders the claim indefinite. The term "substantial" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 2, 5-9, 15-17, and 19 are rejected since they depend

from rejected claims yet do not correct the deficiencies. It is noted that Claims10 and 18 are not included in this rejection since it defines "residual gas space" as not exceeding 15% by volume.

Claims 10 and 18 recite the limitation "the residual gas space" in 7. There is insufficient antecedent basis for this limitation in the claim. The claim is unclear as to whether "the residual gas space" is the same as the "substantial gas space" excluded as recited in line 4 of the claim.

Claims 1-11, 12-14, and 16-17 are indefinite for the recitation "buffer component(s) revealing a buffering action" in Claims 1-4 and 12-14. The claims are unclear as to what is meant by the recitation. Amendment to the claim replacing "revealing" with "having" would overcome this rejection. Claims 5-11 and 16-17 are rejected because they depend from indefinite base claims but do not correct the deficiencies.

Claims 1-11 and 12-19 are indefinite for the recitation that the thrombomodulin solution "is filled aseptically in a container" or "is filed aseptically in a syringe" because solutions are not filled but are used to fill containers.

The term "long period of time" in claims 2-4 and12-14 is a relative term which renders the claim indefinite. The term "long period of time" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 16, 17, 15, 18, and 19 are rejected since they depend from indefinite base claims yet do not correct the deficiencies. Correction is required.

The term "superior in the stability for long term storage" in claims 12, 13, and 14 is a relative term which renders the claim indefinite. The term "superior" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6, 8, 12-15, 18, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Kunihiro et al. (U.S. Patent No. 5,202,421, Apr. 1993).

Kunihiro et al. a thrombomodulin solution and method of its preparation having identical steps to that of the present claims. Since the Kunihiro et al. reference discloses methods with identical steps, it would be inherent that the method would produce identical results as the present invention. Kunihiro et al. describe preparing the thrombomodulin as an aqueous solution having a pH of 7.0 (in the range of 5-7.0) and a phosphate buffer (buffer component) that has buffering action in the pH range of 5 and 7.0. The aqueous solution of thrombomodulin also has a surfactant (LUBROL TM) and is contained in a container (see Col. 9, lines 43-48). The thrombomodulin peptides used in the experiments disclosed by Kunihiro et al. had molecular weights of 72,000, 79,000,

94,000, and 114,000 as determined by SDS-PAGE gel electrophoresis in non-reduced state (Col. 4, lines 54-65). The soluble thrombomodulin of Kunihiro et al. exhibits the function for accelerating the activation of protein C by thrombin and consists of a thrombomodulin which is constituted of an amino acid sequence composed of those amino acid residues in which one or more amino acid residues in the amino acid sequence of SEQ ID NO:1 are replaced or removed or one or more amino acid residues are added thereto (see present clm. 6, part ii). The thrombomodulin solutions of Kunihiro et al. are preferably administered by injection (Col. 10, line 57). The thrombomodulin solutions of Kunihiro et al. would meet the limitations of Claims 12-15, 18, and 19 because they contain all of the components of the compositions of the claims as explained above (thrombomodulin, buffer component at pH 5-7, surfactant and aseptic. It is noted that Claims 12-15 are drawn to compositions and not an apparatus (a syringe, container, etc.). Thus, absent evidence that the components of a composition change with the container they are placed in, the claims drawn to compositions contained in syringes would not be patentably distinguishable from those of Kunihiro et al.

Conclusions

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached on Mon. & Thurs., 8am-5:30pm and Tues. & Wed. 9-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703 308-0196.

Holly Schnizer
June 24, 2002

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